

Supporting Information

Beck et al. 10.1073/pnas.0706527105

SI Text

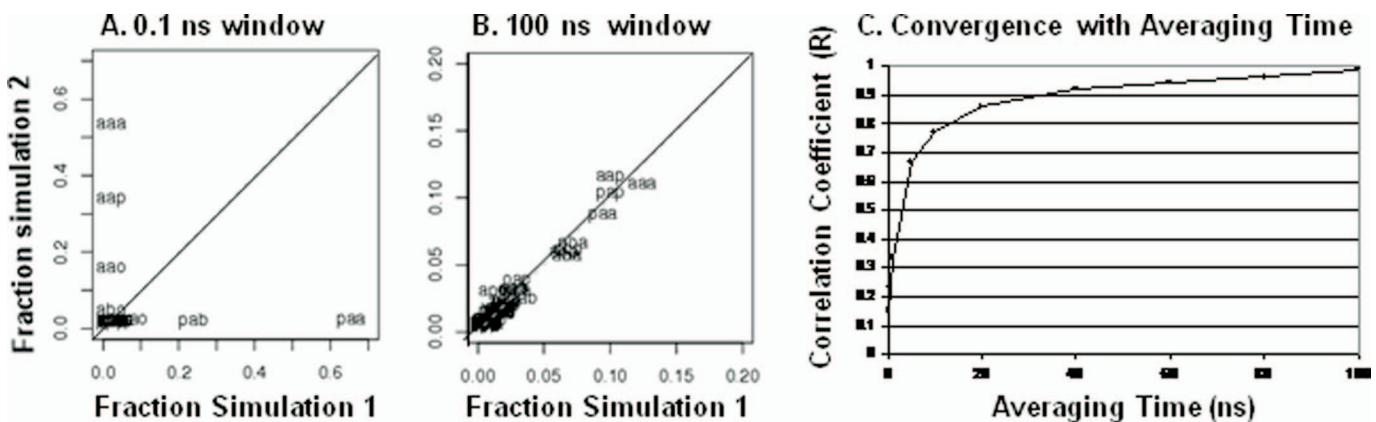


Fig. S1. Convergence properties of conformer populations for the central three residues in GGAGG. (A) Conformers populated during the first nanosecond of two different simulations. If the populations were the same, all of the points would lie on the diagonal. The correlation coefficient is given. The axes reflect the amount of simulation time a triplet was present. (B) Comparison of conformations sampled over the entire 100-ns simulation time of each trajectory. (C) Correlation coefficients for comparison of the two simulations for different time averaging windows over the full trajectories.

Table S1. Conformational properties of Ala in AA and GGAGG peptides with (std q) and without (no q) partial charges and with and without (vac) explicit solvent

aa	sim	Time, ns	By quadrant				By specific conformational region				
			$Q_{\alpha R}$	Q_{β}	$Q_{\alpha L}$	Q_o	α_R	Near α_R	α_L	β	P_{II}
A₁A₂ peptide											
Ala ₁	no q, vac	50	47.4	49.5	2.4	0.8	20.1	19.9	1.6	30.6	17.6
Ala ₁	no q, vac	100	47.4	50.0	1.9	0.7	20.1	19.9	1.2	30.9	17.8
Ala ₂	no q, vac	50	36.5	60.7	2.1	0.6	10.7	18.2	1.3	38.6	22.2
Ala ₂	no q, vac	100	36.4	60.3	2.7	0.6	10.9	18.1	1.7	38.3	22.0
Ala ₁	no q, wat	50	35.5	60.2	3.4	0.9	9.0	17.9	1.9	37.3	20.0
Ala ₁	no q, wat	100	36.0	60.5	2.6	0.8	9.1	18.3	1.3	37.4	20.4
Ala ₂	no q, wat	50	35.6	62.4	1.5	0.6	9.5	17.6	0.5	40.0	21.7
Ala ₂	no q, wat	100	35.0	62.9	1.5	0.6	9.1	17.3	0.5	40.5	22.0
Ala ₁	std q, wat	50	57.6	31.0	11.2	0.2	34.1	17.1	9.4	23.0	18.8
Ala ₁	std q, wat	100	61.4	29.3	9.1	0.2	36.6	18.4	7.5	21.5	17.6
Ala ₂	std q, wat	50	87.9	9.4	2.2	0.4	39.5	38.7	1.8	2.3	2.3
Ala ₂	std q, wat	100	88.8	9.6	1.2	0.4	39.5	39.5	0.9	2.4	2.4
GGAGG peptide											
Ala ₄	no q, vac	50	60.0	38.8	0.5	0.7	22.9	29.9	0.1	5.8	5.5
Ala ₄	no q, vac	100	59.0	38.3	1.9	0.8	22.3	29.4	1.3	6.2	5.6
Ala ₄	no q, wat	50	44.5	52.9	1.9	0.8	12.6	23.5	0.9	24.5	13.6
Ala ₄	no q, wat	100	45.3	52.0	1.9	0.8	12.8	24.1	0.9	23.0	13.0

Table S2. Comparison of proton and heavy atom chemical shifts (in ppm) from experiment* and MD simulations† of GGXGG peptides

Residue	H _N		H _α		H _{β1}		H _{β2}		N _H		C _α		C _β		C'	
	MD	Expt.	MD	Expt.	MD	Expt.	MD	Expt.	MD	Expt.	MD	Expt.	MD	Expt.	MD	Expt.
Ala	8.31 ± 0.55	8.35	4.3 ± 0.32	4.35	1.26 ± 0.04	1.42	123.26 ± 3.49	125.0	52.19 ± 1.48	52.8	21.29 ± 2.14	19.3	175.67 ± 1.50	178.5		
Arg	8.33 ± 0.53	8.39	4.18 ± 0.30	4.38	1.81 ± 0.06	1.91	1.93 ± 0.08	1.79	119.76 ± 3.45	121.2	56.4 ± 1.48	56.5	32.3 ± 1.95	30.9	174.92 ± 1.48	177.1
Asn	8.56 ± 0.53	8.51	4.55 ± 0.23	4.79	2.67 ± 0.04	2.88	2.80 ± 0.06	2.81	119.07 ± 3.00	119.0	54.13 ± 1.50	53.3	41.47 ± 1.57	39.1	173.27 ± 1.37	176.1
Asp	8.50 ± 0.56	8.56	4.56 ± 0.19	4.82	2.62 ± 0.05	2.98	2.65 ± 0.05	2.91	119.84 ± 3.26	119.1	54.33 ± 1.40	53.0	43.67 ± 1.69	38.3	174.3 ± 1.60	175.9
Cys	8.40 ± 0.52	8.44	4.41 ± 0.27	4.59	2.95 ± 0.06	2.98	2.92 ± 0.06	2.98	119.31 ± 3.66	118.8	59.62 ± 1.62	58.6	33.05 ± 2.35	28.3	172.39 ± 1.33	175.3
Gln	8.43 ± 0.54	8.44	4.19 ± 0.33	4.38	2.04 ± 0.05	2.17	2.11 ± 0.08	2.01	119.66 ± 3.24	120.5	56.12 ± 1.52	56.2	31.14 ± 1.83	29.5	174.39 ± 1.58	176.8
Glu	8.54 ± 0.54	8.40	4.25 ± 0.29	4.42	1.96 ± 0.05	2.18	1.94 ± 0.08	2.01	120.55 ± 3.25	120.2	56.55 ± 1.53	56.1	31.72 ± 1.70	29.9	175.01 ± 1.52	176.8
Gly	8.48 ± 0.64	8.41	3.83 ± 0.31	4.02	3.11 ± 0.07	3.35	3.27 ± 0.08	3.19	118.52 ± 3.61	118.1	56.0 ± 1.49	55.4	31.67 ± 1.99	29.1	171.73 ± 1.69	174.9
His	8.45 ± 0.52	8.56	4.55 ± 0.30	4.79	3.11 ± 0.07	3.35	3.27 ± 0.08	3.19	118.52 ± 3.61	118.1	56.0 ± 1.49	55.4	31.67 ± 1.99	29.1	173.25 ± 1.62	175.1
Ile	7.99 ± 0.52	8.17	4.22 ± 0.27	4.21	1.87 ± 0.04	1.89	114.98 ± 4.19	120.4	60.23 ± 1.32	61.6	40.24 ± 1.09	38.9	174.31 ± 1.27	177.1		
Leu	8.24 ± 0.51	8.28	4.25 ± 0.33	4.38	1.63 ± 0.05	1.67	1.67 ± 0.07	1.62	121.15 ± 3.17	122.4	55.21 ± 1.52	55.5	43.99 ± 1.73	42.5	175.41 ± 1.55	178.2
Lys	8.38 ± 0.53	8.36	4.22 ± 0.25	4.36	1.75 ± 0.05	1.89	1.81 ± 0.08	1.77	120.19 ± 3.15	121.6	56.56 ± 1.48	56.7	34.58 ± 1.77	33.2	175.29 ± 1.47	177.4
Met	8.42 ± 0.55	8.42	4.08 ± 0.56	4.52	2.03 ± 0.07	2.15	2.07 ± 0.07	2.03	120.29 ± 3.42	120.3	55.63 ± 1.49	55.8	33.8 ± 2.10	32.9	174.94 ± 1.37	177.1
Phe	8.41 ± 0.61	8.31	4.53 ± 0.30	4.65	2.95 ± 0.11	3.19	2.97 ± 0.11	3.04	120.25 ± 3.64	120.7	57.83 ± 1.62	58.1	41.9 ± 1.69	39.8	173.92 ± 1.50	176.6
Pro			4.3 ± 0.14	4.45	2.14 ± 0.06	2.29	2.07 ± 0.05	1.99			63.43 ± 1.15	63.7	32.73 ± 0.69	32.2	174.68 ± 1.20	177.8
Ser	8.4 ± 0.51	8.43	4.34 ± 0.29	4.51	3.89 ± 0.06	3.95	3.87 ± 0.08	3.90	116.96 ± 3.36	115.5	58.64 ± 1.50	58.7	64.91 ± 1.59	64.1	172.85 ± 1.46	175.4
Thr	8.15 ± 0.49	8.25	4.26 ± 0.29	4.43	4.24 ± 0	4.33			115.62 ± 3.89	112.0	62.54 ± 1.27	62.0	71.17 ± 1.47	70.0	172.91 ± 1.25	175.6
Trp	8.29 ± 0.49	8.22	4.27 ± 0.41	4.70	2.48 ± 0.06	3.34	2.29 ± 0.06	3.25	123.92 ± 6.05	122.1	57.1 ± 1.58	57.6	31.75 ± 2.05	29.8	174.5 ± 1.58	177.1
Tyr	8.19 ± 0.61	8.26	4.34 ± 0.40	4.58	2.93 ± 0.1	3.09	2.9 ± 0.1	2.97	119.32 ± 3.61	120.9	57.9 ± 1.51	58.3	40.74 ± 2.04	38.9	173.62 ± 2.32	176.7
Val	8.06 ± 0.50	8.16	4.03 ± 0.29	4.16	2.08 ± 0	2.11			116.7 ± 4.62	119.3	61.73 ± 1.95	62.6	34.25 ± 1.32	31.8	174.41 ± 1.30	177.0

*Experimental values were taken from ref. 1.

†MD-predicted values calculated with ShiftX v1.0 (17) from PDB files produced from simulation at 1 ps granularity. The last 50 ns of simulation time were used for these calculations.

1. Schwarzeniger S, Kroon GJA, Foss TR, Wright PE, Dyson HJ (2000) Random coil chemical shifts in acidic 8 M urea: Implementation of random coil shift data in NMRView. *J Biomol NMR* 18:43–48.

Table S3. Correlations between chemical shifts calculated from MD simulations* and those observed experimentally†

	<i>R</i>	Values
H _N	0.8666	19
H _α	0.8703	20
H _{β1}	0.9722	19
H _{β2}	0.9216	15
N _H	0.8483	19
C _α	0.9879	20
C _β	0.9950	19
C'	0.9068	20
Overall	0.9998	151

*Predictions calculated with ShiftX v1.0 (17) from PDB files produced from neutral pH, 298 K simulations at 1 ps granularity. The last 50 ns of simulation time were used for these calculations.

†Experimental data were taken from table 1 in Schwarzinger *et al.* (1). Conditions are 8 M urea, pH 2.3 and 293 K.

- Schwarzinger S, Kroon GJA, Foss TR, Wright PE, Dyson HJ (2000) Random coil chemical shifts in acidic 8 M urea: Implementation of random coil shift data in NMRView. *J Biomol NMR* 18:43–48.

Table S4. Correlations between MD-derived predicted and experimentally observed proton chemical shifts for GGXGG peptides

Correlation coefficient, <i>R</i>	Ref. 1*	Ref. 2†	Ref. 2‡	Ref. 3§	MD (SHIFTS)¶	MD (ShiftX)
Schwarzinger <i>et al.</i> *	1	0.999	0.999	0.999	0.999	0.997
Plaxco <i>et al.</i> †	0.999	1	0.999	0.999	0.999	0.997
Plaxco <i>et al.</i> ‡	0.999	0.999	1	0.999	0.999	0.997
Merutka <i>et al.</i> §	0.999	0.999	0.999	1	0.998	0.998
MD (SHIFTS)¶	0.999	0.999	0.999	0.998	1	0.996
MD (ShiftX)	0.997	0.997	0.997	0.998	0.996	1

*Experimental data taken from table 1 of Schwarzinger *et al.* (1). Conditions are 8 M urea, pH 2.3 and 293 K.

†Experimental data taken from table 2 of Plaxco *et al.* (2). Conditions are 6 M GuHCl, pH 5.0 and 293 K.

‡Extrapolated data taken from table 2 of Plaxco *et al.* (2). Extrapolations to 0 M GuHCl, pH 5.0 and 293 K.

§Experimental data taken from table 2 of Merutka *et al.* (3). Conditions are 90% H₂O / 10% D₂O, pH 5.0 at 277.2 K.

¶SHIFTS version 4.1.4 (4) was used to calculate the chemical shifts from the MD-generated ensembles. Cys, His, and Pro were not included because of difficulties with SHIFTS. There were a total of 62 values included in these calculations.

||ShiftX version 1.0 (5) was used to calculate the chemical shifts from the MD-generated ensembles. There were a total of 73 values included in these calculations, except those against the smaller SHIFTS data.

1. Schwarzinger S, Kroon GJA, Foss TR, Wright PE, Dyson HJ (2000) Random coil chemical shifts in acidic 8 M urea: Implementation of random coil shift data in NMRView. *J Biomol NMR* 18:43–48.
2. Plaxco KW, *et al.* (1997) The effects of guanidine hydrochloride on the “random coil” conformations and NMR chemical shifts of the peptide series GGXGG. *J Biomol NMR* 10:221–230.
3. Merutka G, Dyson HJ, Wright PE (1995) “Random coil” ¹H chemical shifts obtained as a function of temperature and trifluoroethanol concentration for the peptide series GGXGG. *J Biomol NMR* 5:14–24.
4. Osapay K, Case DA (1991) *J Am Chem Soc* 113:9436–9444.
5. Neal S, Nip AM, Zhang H, Wishart DS (2003) Rapid and accurate calculation of protein ¹H, ¹³C and ¹⁵N chemical shifts. *J Biomol NMR* 26:215–240.

Table S5. MD-derived helix propensity scales (helical free energies relative to all other conformers) compared with consensus experimental propensity scale from multiple host-guest studies

Residue	Consensus experimental propensities (1)	$\Delta G_{\alpha R, MD}$ in GGXGG	$\Delta G_{\alpha R, MD}$ in native proteins
Ala	0	0.70	-0.01
Arg	0.21	0.56	0.17
Leu	0.21	0.35	0.10
Met	0.24	0.47	0.18
Lys	0.26	0.43	0.16
Gln	0.39	0.60	0.06
Glu	0.40	0.45	0.04
Ile	0.41	0.97	0.36
Trp	0.49	0.48	0.23
Ser	0.50	0.55	0.36
Tyr	0.53	0.64	0.43
Phe	0.54	0.53	0.42
His	0.56	0.66	0.52
Val	0.61	0.76	0.46
Asn	0.65	0.23	0.35
Thr	0.66	0.77	0.36
Cys	0.68	0.54	0.27
Asp	0.69	0.48	0.40
Gly	1.00	0.96	0.92
Pro	3.16	0.89	0.47

Correlation coefficient (R); $R = 0.28$; $R = 0.84$ or 0.92 , omitting Pro.

1. Pace CN, Scholtz JM (1998) A helix propensity scale based on experimental studies of peptides and proteins. *Biophys J* 75:422–427.